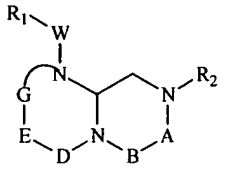
CLAIMS

We claim:

1. A compound having the following general formula (I):



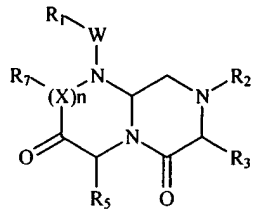
(I)

wherein A is -(CHR_3)- or -(C=O)-, B is -(CHR_4)-, -(C=O)-, D is –(CHR_5)- or –(C=O)-, E is –(ZR_6)-, -(C=O)-, G is –(XR_7)$_n$-, -(CHR_7)-(NR_8)-, -(C=O)-(XR_9)-, or -(C=O)-, W is -Y(C=O)-, -(C=O)NH-, -(SO_2)- or nothing, Y is oxygen, sulfur or -NH-, X and Z is independently nitrogen or CH, n=0 or 1; and R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 are the same or different and independently selected from an amino acid side chain moiety or derivative thereof, the remainder of the molecule, a linker and a solid support, and stereoisomers thereof.

2. The compound of claim 1, wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 are independently selected from the group consisting of aminoC_{2-5}alkyl, guanidinoC_{2-5}alkyl, C_{1-4}alkylguanidinoC_{2-5}alkyl, diC_{1-4}alkylguanidino-C_{2-5}alkyl, amidinoC_{2-5}alkyl, C_{1-4}alkylamidinoC_{2-5}alkyl, diC_{1-4}alkylamidinoC_{2-5}alkyl, C_{1-3}alkoxy, Phenyl, substituted phenyl(where the substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), benzyl, substituted benzyl (where the substituents on the benzyl are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), naphthyl, substituted naphthyl (where the substituents are independently selected from one or more of amino, amidino,

guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), bis-phenyl methyl, substituted bis-phenyl methyl (where the substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), pyridyl, substituted pyridyl, (where the substituents are independently selected from one or more of amino amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), pyridylC_{1-4}alkyl, substituted pyridylC_{1-4}alkyl (where the pyridine substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), pyrimidylC_{1-4}alkyl, substituted pyrimidylC_{1-4}alkyl (where the pyrimidine substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy or nitro, carboxy, cyano, sulfuryl or hydroxyl), triazin-2-yl-C_{1-4}alkyl, substituted triazin-2-yl-C_{1-4}alkyl (where the triazine substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), imidazoC_{1-4}alkyl, substituted imidazol C_{1-4}alkl (where the imidazole sustituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), imidazolinylC_{1-4}alkyl, N-amidinopiperazinyl-N-C_{0-4}alkyl, hydroxyC_{2-5}alkyl, C_{1-5}alkylaminoC_{2-5}alkyl, hydroxyC_{2-5}alkyl, C_{1-5}alkylaminoC_{2-5}alkyl, C_{1-5}dialkylaminoC_{2-5}alkyl, N-amidinopiperidinylC_{1-4}alkyl and 4-aminocyclohexylC_{0-2}alkyl.

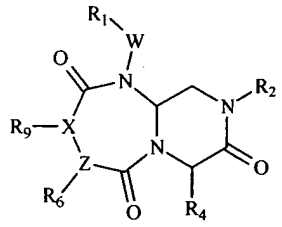
3. The compound of claim 1, wherein A is $-(CHR_3)-$, B is $-(C=O)-$, D is $-(CHR_5)-$, E is $-(C=O)-$, G is $-(XR_7)_n-$, and the compound has the following general formula (II):



(II)

wherein R_1, R_2, R_3, R_5, R_7, W, X and n are as defined in claim 1.

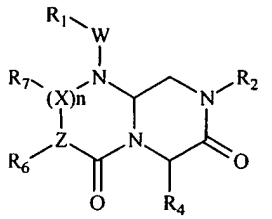
4. The compound of claim 1, wherein A is $-(C=O)-$, B is $-(CHR_4)-$, D is $-(C=O)-$, E is $-(ZR_6)-$, G is $-(C=O)-(XR_9)-$, and the compound has the following general formula (III):



(III)

wherein R_1, R_2, R_4, R_6, R_9, W and X are as defined in claim 1, Z is nitrogen or CH (when Z is CH, then X is nitrogen).

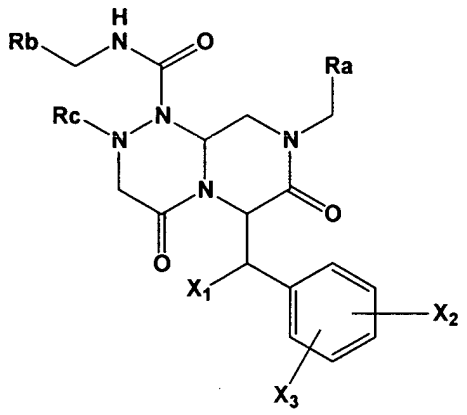
5. The compound of claim 1, wherein A is $-(C=O)-$, B is $-(CHR_4)-$, D is $-(C=O)-$, E is $-(ZR_6)-$, G is $(XR_7)_n-$, and the compound has the following general formula (IV):



(IV)

wherein R_1, R_2, R_4, R_6, R_7, W, X and n are as defined in claim 1, and Z is nitrogen or CH, with the proviso that when Z is nitrogen, then n is zero, and when Z is CH, then X is nitrogen and n is not zero.

6. The compound of claim 5, wherein the compound has the following general formula (VI):



wherein R_a is a phenyl group; a substituted phenyl group having one or more substituents wherein the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl groups; a benzyl group; a substituted benzyl group with one or more substituents where the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl group; or a bicyclic aryl group having 8 to 11 ring members, which may have 1 to 3 heteroatoms selected from nitrogen, oxygen or sulfur; R_b is a monocyclic aryl group having 5 to 7 ring members, which may have 1 to 2 heteroatoms selected from nitrogen, oxygen or sulfur, and aryl ring in the compound may have one or more substituents selected from a group consisting of halide, hydroxy, cyano, lower alkyl, and lower alkoxy groups; Rc is a saturated or unsaturated C_{1-6}alkyl,

C_{1-6}alkoxy, perfluoro C_{1-6}alkyl group; and X_1, X_2, and X_3 may be the same or different and independently selected from hydrogen, hydroxyl, and halide.

7. The compound of claim 6, wherein R_a is a wherein R_a is a phenyl group; a substituted phenyl group having one or more substituents wherein the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl groups; a benzyl group; a substituted benzyl group with one or more substituents where the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl group; a naphthyl group; a quinolinyl group; or an isoquinolinyl group; and R_b is phenyl, pyridyl or piperidyl, all of which may be substituted with one or more substituents selected from a group consisting of halide, hydroxy, cyano, lower alkyl, and lower alkoxy groups.

8. The compound of claim 6, wherein R_a is wherein R_a is a phenyl group; a substituted phenyl group having one or more substituents wherein the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl groups; a benzyl group; a substituted benzyl group with one or more substituents where the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl group; or a naphthyl group; and R_b is phenyl, which may be substituted with one or more substituents selected from a group consisting of halide, hydroxy, cyano, lower alkyl, and lower alkoxy group.

9. The compound of claim 1, wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 or R_9 is joined to a solid support or solid support derivatives.

10. The compound of claim 2, wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 or R_9 is joined to a solid support or solid support derivatives.

11. The compound of claim 3, wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 or R_9 is joined to a solid support or solid support derivatives.

12. A pharmaceutical composition comprising a compound according to any one of claims 1-8 and pharmaceutically acceptable carrier.

13. A pharmaceutical composition of claim 12, the composition comprising a safe and effective amount of the compound.

14. A library of compounds, comprising at least one compound according to any one of claims 1-8.

15. A method of identifying a biologically active compound, comprising contacting the library of claim 14 with a target to detect or screen the biologically active compound.

16. A method for carrying out a binding assay, comprising:

a) providing a composition comprising a first co-activator and an interacting protein, said first co-activator comprising a binding motif of LXXLL, LXXLI or FXXFF wherein X is any amino acid;

b) combining the first co-activator and the interacting protein with a test compound; and

c) detecting alteration in binding between the first co-activator and the interacting protein in the presence of the compound;
wherein the test compound is selected from a compound of any one of claims 1-8.

17. The method of claim 16, wherein said interacting protein is a transcription factor or a second co-activator.

18. The method of claim 16, wherein said interacting protein is selected from the group consisting of RIP140; SRC-1 (NCoA-1); TIF2 (GRIP-1; SRC-2); p (CIP; RAC3; ACTR; AIB-1; TRAM-1; SRC-3); CBP (p300); TRAPs (DRIPs); PGC-1; CARM-1; PRIP (ASC-2; AIB3; RAP250; NRC); GT-198; and SHARP (CoAA; p68; p72).

19. The method of claim 16, wherein said interacting protein is selected from the group consisting of TAL 1; p73; MDm2; TBP; HIF-1; Ets-1; RXR; p65; AP-1; Pit-1; HNF-4; Stat2; HPV E2; BRCA1; p45 (NF-E2); c-Jun; c-myb; Tax; Sap 1; YY1; SREBP; ATF-1; ATF-4; Cubitus; Interruptus; Gli3; MRF; AFT-2; JMY; dMad; PyLT: HPV E6; CITTA; Tat; SF-1; E2F; junB; RNA helicase A; C/EBP β; GATA-1; Neuro D; Microphthalimia; E1A; TFIIB; p53; P/CAF; Twist; Myo D; pp9O RSK; c-Fos; and SV40 Large T.

20. The method of claim 16, wherein said interacting protein is selected from the group consisting of ERAP140; RIP140; RIP160; Trip1; SWI1 (SNF); ARA70; RAP46; TIF1; TIF2; GRIP1; and TRAP.

21. The method of claim 16, wherein said interacting protein is selected from the group consisting of VP16; VP64; p300; CBP; PCAF; SRC1 PvALF; AtHD2A; ERF-2; OsGAI; HALF-1; C1; AP-1; ARF-5; ARF-6; ARF-7; ARF-8; CPRF1; CPRF4; MYC-RP/GP; and TRAB1.

22. The method of claim 16, wherein said first co-activator is CBP or p300.

23. A method for inhibiting tumor growth comprising administering to a mammalian subject having a tumor a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, in an amount effective to inhibit the growth of the tumor in the mammalian subject.

24. The method of claim 23 wherein the tumor is cancerous.

25. The method of claim 23 wherein the tumor is colorectal cancer.

26. A method of treating or preventing cancer comprising administering to a subject in need thereof a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, in an amount effective to treat or prevent the cancer.

27. The method of claim 26 wherein the cancer is colorectal cancer.

28. The method of claim 26 wherein the compound or the composition is administered in combination with an anti-neoplastic agent.

29. The method of claim 28 wherein the anti-neoplastic agent is selected from the group consisting of 5-FU, taxol, cisplatin, mitomycin C, tegafur, raltitrexed, capecitabine, and irinotecan.

30. A method of treating or preventing restenosis associated with angioplasty comprising administering to a subject in need thereof an amount of a

compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, where the amount is effective to prevent the restenosis.

31. A method of treating or preventing polycystic kidney disease comprising administering to a subject in need thereof an amount of a compound according to any one of claims 1-8, or a composition according to claims 12 or 13, where the amount is effective to treat the polycystic kidney disease.

32. A method of treating or preventing aberrant angiogenesis disease comprising administering to a subject in need thereof an amount of a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, where the amount is effective to treat the aberrant angiogenesis disease.

33. A method of treating or preventing rheumatoid arthritis disease comprising administering to a subject in need thereof an amount of a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, where the amount is effective to treat the rheumatoid arthritis disease.

34. A method of treating or preventing ulcerative colitis comprising administering to a subject in need thereof an amount of a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, where the amount is effective to treat the ulcerative colitis.

35. A method for treating or preventing tuberous sclerosis complex (TSC) comprising administering to a subject in need thereof an amount of a compound of any of claims 1-8, or a composition of claim 12 or claim 13, where the amount is effective to treat or prevent TSC.

36. A method for treating or preventing a KSHV-associated tumor comprising administering to a subject in need thereof an amount of a compound of any of claims 1-8, or a composition of claim 12 or claim 13, where the amount is effective to treat or prevent the KSHV-associated tumor.

37. A method for modulating hair growth comprising administering to a subject in need thereof an amount of a compound of any of claims 1-8, or a composition of claim 12 or claim 13, where the amount is effective to modulate hair growth on the subject.

38. A method of treating or preventing Alzheimer's disease comprising administering to a subject in need thereof an amount of a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, where the amount is effective to treat or prevent Alzheimer's disease.

39. A method for promoting neurite outgrowth, comprising contacting a neuron with a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, in an amount effective to promote neurite outgrowth.

40. A method for promoting differentiation of a neural stem cell comprising contacting a neural stem cell with a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, where the amount is effective to promote differentiation of the neural stem cell.

41. A method for promoting apoptosis in cancer cells comprising contacting cancer cells with a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, in an amount effective to promote apoptosis in the cancer cells.

42. A method for inhibiting survivin expression in a cell comprising contacting a survivin-expressing cell with a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, in an amount effective to inhibit survivin expression.